way pressures generated, particularly when the lungs are noncompliant. This may lead to various forms of barotrauma (such as pneumothorax or subcutaneous and mediastinal emphysema) as well as cardiovascular effects, including a reduction in cardiac output and blood pressure or an increase in venous pressure leading to raised intracranial pressures, hepatic engorgement or increased renal vascular resistance. Further, it is often difficult to synchronize a patient's breathing with a ventilator without resorting to the use of sedatives, narcotics or muscle relaxants, all of which have certain risks and which obscure useful clinical information, particularly in the presence of neurological disease. Thus, alternative methods of ventilation, including high frequency positive pressure ventilation (HFPPV), have been studied.

There are many devices used for HFPPV (at present each investigator must build his own); however, all are designed to deliver small tidal volumes (less than 3 ml per kg of body weight) at rates which vary from 60 to 2,400 breaths per minute (1 to 40 Hz). At lower rates (less than 5 Hz), most systems employ an "open" circuit with a pulsatile jet of gas injected into the airway by way of an open endotracheal tube or transtracheally. Conventional closed, valved circuits can be used if the ventilator is equipped with small diameter, noncompliant tubing, having minimal compression volumes, and if it has a high-rate capability. High frequency oscillation (HFO) machines may either use a similar technology or employ a simple to-and-fro piston with a single hose circuit by which fresh gas is delivered near the patient (similar to a Mapleson D). With this method, carbon dioxide absorption is unnecessary.

The classic view of respiratory physiology states that very low volumes lead to atelectasis and accumulation of carbon dioxide (because only the "dead space" is ventilated). However, this has been disproved repeatedly by studies using the high frequency ventilation systems. These systems are capable of providing long-term support with normal gas exchange and without evidence of atelectasis, in spite of peak airway pressures of less than 5 to 8 cm of water. However, in the presence of severe lung disease PEEP may still be needed. Gas exchange does not depend on bulk gas movement (hence, anatomical dead space becomes less important); instead it acts as "facilitated diffusion" in which agitation of the intrathoracic gas constantly mixes fresh and alveolar gases.

HFPPV and HFO methods have many advantages. Lower airway pressures may minimize the risks of barotrauma and clearly reduce air leaks from bronchopleural fistulas, thus promoting healing. They may also prove useful in supporting patients following pneumonectomy in whom there is a risk of bronchial stump disruption. These lower pressures may improve cardiac output although this can be offset if PEEP is required. Several groups claim that clearance of secretions is enhanced, possibly because the constant vibration is percussive. Another benefit is the reflex suppression of spontaneous respiratory drive (without hyperventilation), perhaps due to an alteration in stretch receptor stimulation, which can minimize the need for sedatives and ease patient acceptance of the ventilator. This may not be true in the presence of very severe lung disease although some devices also allow simultaneous, spontaneous breathing during HFPPV. HFPPV may also reduce ventilatory-synchronous movement of various organs (such as the brain, lung and diaphragm) making the surgical procedure easier.

High frequency techniques represent a major new approach to mechanical ventilation, although commercial equipment is not yet available. However, it will be several years before all of the benefits and disadvantages are known and the physiology completely understood.

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Isoflurane: A New Inhalation Anesthetic

ISOFLURANE (FORANE) was first synthesized in 1965 by Ross C. Terrell of Ohio Medical Products, following the development of its isomer, enflurane (Ethrane), which has been in clinical use since 1973. Isoflurane has undergone extensive studies in animals and in humans and has been approved by the Food and Drug Administration for use in the United States. It is also used in Canada.

Isoflurane, a fluorinated ether, is a nonflammable, clear, colorless, stable liquid that contains no additives or chemical stabilizers. Induction of

isoflurane is fairly rapid at 1 percent to 4 percent inspired concentration. This agent has mild pungency, which may limit the rate of induction in some patients, although excessive salivation or tracheobronchial secretions do not appear to be stimulated. The depth of anesthesia can be easily altered by controlling the inspired anesthetic concentration. Recovery from anesthesia is usually smooth and rapid, and no significant incidence of nausea or vomiting has been observed.

Anesthesia is maintained with 0.8 percent to 2 percent inspired concentration of isoflurane. The agent is a potent respiratory depressant and, hence, respiratory status needs to be closely monitored and supported when necessary. This depression is partially reversed by surgical stimulation. Systemic blood pressure decreases with induction of anesthesia as a result of a decline in the peripheral vascular resistance, an effect similar to that of enflurane and halothane. Blood pressure returns toward normal values on commencement of the surgical stimulation. With regard to its cardiac effects, isoflurane is superior to both enflurane and halothane because it does not decrease myocardial function or cardiac output during moderate depth of anesthesia. Isoflurane does not appear to sensitize the myocardium to catecholamines (epinephrine). There is a modest increase in heart rate under isoflurane, irrespective of the anesthetic concentration. This effect is in contrast to that of enflurane, which produces a dose-related increase in heart rate and that of halothane, which causes no increase in heart rate. Isoflurane is free from the central nervous system excitatory properties of its isomer, enflurane. It produces excellent muscle relaxation as does enflurane, is roughly two to three times more effective than halothane, and greatly potentiates all muscle relaxants.

Of all the halogenated anesthetic agents, isoflurane is the least metabolized in humans or animals. This relative stability strongly indicates that the agent should have no potential to produce organ toxicity. Studies carried out in humans and animals also suggest little or no effect on the liver or kidney, and there is no evidence to indicate the carcinogenicity of isoflurane.

Isoflurane claims superiority over several other inhalation anesthetics for its effect on the cardiovascular system, the central nervous system, the neuromuscular system, anesthetic metabolism and organ toxicity. Its drawbacks include a pungent smell, considerable respiratory depression, tachycardia and hypotension. The full potency of this anesthetic agent will not be known until it is administered to several thousand patients for various surgical procedures. Isoflurane is not perfect, but it comes one step closer to being an ideal inhalation anesthetic agent.

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The Role of Ketamine in Obstetric Anesthesia

DESPITE INITIAL FAVORABLE EVALUATION of therapy with low doses of ketamine (0.5 mg per kg of body weight) in obstetric patients, the drug has not been widely used during delivery for two reasons: First, several subsequent investigators showed significant neonatal depression with higher doses (2 to 5 mg per kg of body weight) of the drug. Although later evidence showed that low doses (0.2 to 0.4 mg per kg of body weight) did not have a substantial depressant effect on newborn infants, the decline in ketamine's use caused by the earlier results persisted. Second, there is a growing, and laudable, trend away from the use of general anesthesia in obstetrics. Consequently, there is no indication for the large doses of ketamine (1 to 2 mg per kg of body weight) used to induce general anesthesia.

Ketamine is becoming more popular as an intravenously administered *analgesic* for the second and third stages of labor. When very low doses of the drug are given women for whom regional or inhalational methods of analgesia are unsuitable, consciousness and patient cooperation are maintained and relief of pain is excellent. Because the mother retains her protective airway reflexes, endotracheal intubation is not required, and high flows of oxygen can be administered by face mask. Some of the other problems often associated with larger doses of ketamine are not seen with the low-dose technique. For example, hypertension and tachycardia occur only rarely, and bad dreams or hallucinations are similarly infrequent.

Two intravenous doses of 5 to 10 mg of